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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JAN E. SCHNITZER

Appeal 2009-001909
Application 10/056,230
Technology Center 1600

Decided:[1] July 7, 2009

Before DEMETRA J. MILLS, LORA M. GREEN, and MELANIE L. McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method for delivering an agent across a luminal surface of vascular endothelium. The Examiner has rejected the claims as nonenabled and not being supported

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

by an adequate written description. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 3-5, 7-9, and 12-14 are on appeal (App. Br. 2). Claims 2, 6, 10, 11, and 15-17 are also pending but have been withdrawn from consideration by the Examiner (*id.*).

The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). We will focus on claims 3, 4, 12, and 14, which read as follows:

3. A method of delivering an agent of interest across a luminal surface of vascular endothelium and from one side of an underlying cell to another side in a tissue-specific manner, comprising the steps of:

a) selecting an agent of interest that binds to and localizes to a component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface, wherein the component to which the agent binds and localizes is tissue specific; and

b) contacting the luminal surface of vasculature with the agent of interest, thereby delivering the agent across the luminal surface of the vascular endothelium and from one side of an underlying cell to another side in a tissue-specific manner.

4. The method of Claim 3, wherein the agent of interest comprises an active agent component and a transport agent component, wherein the transport agent component binds to and localizes to a component of caveolae of the luminal surface of the vascular endothelium.

12. The method of claim 4, wherein the transport agent component is selected from the group consisting of: an antibody, a peptide, an inactivated virus, a receptor, a ligand and a nucleic acid.

14. The method of claim 4, wherein the tissue is selected from the group consisting of: vascular, pulmonary, cardiac, cerebral, nephric, hepatic, endocrinous and intestinal tissue.

Claims 3-5, 7-9, and 12-14 stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification . . . does not reasonably provide enablement for a method of delivering any agent of interest across a luminal surface of vascular endothelium from one side of an underlying cell to another side in a tissue specific manner" (Ans. 4).

Claims 3-5, 7-9, and 12-14 stand rejected under 35 U.S.C. § 112, first paragraph, "as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" (Ans. 6).

ISSUES

Has Appellant demonstrated that the Examiner erred in concluding that claim 3 is not enabled?

Has Appellant demonstrated that the Examiner erred in concluding that claim 3 is not supported by an adequate written description?

FINDINGS OF FACT

1. "Continuous endothelium contain distinct flask-shaped invaginations in the plasma membrane called caveolae that are open to the luminal blood vessel space where circulating molecules may enter them" (Spec. 2).

2. The Specification describes "methods of purifying microdomains of plasma membranes, including caveolae, . . . as well as the resulting purified microdomains and uses therefor" (*id.* at 3-4).

3. The Specification also discloses:

> Caveolae . . . can be used to identify mechanisms or routes by which molecules can be delivered into cells, particularly

> endothelial cells. . . . For example, . . . molecules residing in caveolae can be targeted by antibodies or natural ligands to caveolar proteins or receptors, thereby bringing agents conjugated to the antibody or ligand to, into, and/or across the endothelium.

(*Id.* at 4.)

4. The Specification, in Examples 1 and 2 and Figure 1, discloses obtaining "purified caveolae . . . from isolated luminal endothelial cell plasma membranes" (*id.* at 6 & 22-26).

5. The Specification states:

> The purified caveolae . . . are useful for the identification of molecules and proteins which are involved in intra- or trans-cellular transport. . . . For example, purified caveolae can be used to generate antibodies, either monoclonal or polyclonal, using standard techniques. . . . Once the antibodies are raised, they are assessed for the ability to bind to purified caveolae. Conventional methods can be used to perform this assessment.

(*Id.* at 11.)

6. The Specification also discloses that "[a]ntibodies as described above can be used to identify further the proteins associated with intra- and trans-cellular transport: for example, the antibodies can be applied to endothelium in order to determine whether they interfere with transport in endothelium." (*Id.* at 13.)

7. The Specification also discloses:

> Antibodies can additionally be used as vectors to deliver agents into and/or across the endothelium. For example, as described in Examples 8 and 9 below, monoclonal antibodies have been generated which recognize antigens found primarily in purified caveolae, and which can be used for tissue-specific transcytosis *in vivo*. Most of the antibodies recognize endothelia; a few are specific for continuous endothelia. Furthermore, antibodies can

> be generated which are tissue specific. Two of the antibodies described in Example 8 recognize lung tissue. Tissue-specific antibodies can be used as transport agents to deliver agents, such as antibodies, drugs, genes, diagnostic agents, or other molecules to a specific tissue, and particularly to the caveolae of a specific tissue, so that the agents can be delivered to and/or across the endothelium.

(*Id.* at 13.)

8. The Specification also discloses:

> Directing delivery of a drug or other agent which is to enter a cell through the action of caveolae . . . can be carried out by using as a "probe" or transporting molecule a molecule (such as an antibody, a peptide, a virus, a ligand) which has a relatively high affinity interaction with a component of caveolae.

(*Id.* at 17.) However, the Specification does not provide examples where the transporting molecule is a peptide, a virus, or a ligand other than an antibody.

9. The Specification also discloses:

> Proteins and other components of caveolae . . . which can be targets for the probes or transporting molecules can be identified using purified caveolae . . . of the present invention. . . . To identify such molecules, standard assays can be used, including: two-dimensional gel analysis followed by microsequencing, Western blotting with antibodies to known proteins (as described herein), or blotting with antibodies as described above.

(*Id.* at 17.)

10. In Example 8, the Specification discloses the generation of monoclonal antibodies to plasma membranes and caveolae of endothelium in situ (*id.* at 36). In particular, the Specification states:

Luminal endothelial cell plasma membrane was purified along with its caveolae directly from rat lung tissue by in situ coating procedures. . . . Monoclonal antibodies were generated by standard techniques, using 100 μg of [the luminal endothelial membrane] as immunogen. Over 100 hybridomas were raised that recognize by ELISA the silica-coated luminal endothelial cell plasma membranes adsorbed onto 96-well trays. Twenty stable clones were established and their mAbs analyzed by Western blotting and tissue immunocytochemistry. . . .

Seven [of the] mAbs (833, 472, 154, 228, 302, 309 and another mAb) recognized antigens found primarily in purified caveolae (V), based on their enrichment in (V) but near complete absence from [the membrane remaining after removal of (V)]. Two of these antibodies (833 and 472) reacted with the surface of microvascular endothelium in lung tissue, as assessed by both immunoblotting and tissue immunostaining. Antibodies 833 and 472 appeared to be monospecific for proteins in [the membrane] of about 85 and 90 kDa, respectively. Densitometry revealed that both antigens were very enriched in [the luminal endothelial membrane] over the starting lung homogenate (H) (78- fold for 833, and 23-fold for 472) and also in the purified caveolae (V) over the silica-coated membrane stripped of caveolae (P-V) (60-fold for 833 and 7-fold for 472). In addition, significant co-localization was found on the cell surface of the signal of 833 and 472 with that of caveolin recognized by commercially available antibodies. . . .

Based on the initial tissues tested (lung, heart, brain, liver, kidney, adrenal, testes, intestine, skeletal muscle, and spleen), both Western blotting of whole tissue lysates and immunohistochemical staining of formaldehyde-fixed tissue sections indicated good lung specificity for both 833 and 472. They reacted with the endothelium only in lung tissue and did not stain larger blood vessels, suggesting microvascular specificity. . . . In contrast, many of the other monoclonal antibodies stained endothelia in many different tissues and in both large and small blood vessels. Screening of rat organs

> indicated that most of these mAbs recognized all endothelia, whereas a few were specific for continuous endothelia.

(*Id.* at 36-38.)

11. The Specification, in Example 8, additionally discloses that "more organ- and caveolae-specific antibodies (833, 472, 154, 228, 302 and 309) are being examined further" (*id.* at 38). In particular, the Specification discloses:

> Each different antibody was injected into three different rats, with nearly identical results. The nontargeting negative control antibody had low reactivity and remained primarily intravascular, as indicated by very high counts in the blood. As expected, the liver had the most significant uptake of this antibody. Conversely, both 472 and 833 had very low blood counts (> 10-fold less than the control for 833) and very significant tissue uptake in the lung (>50-fold for 833 over the control). Both showed similar low levels of uptake in the liver. . . . Most importantly, mAb 833 appeared specifically to accumulate most rapidly and significantly in the lung with very little detection in other organs. . . .
>
> In light of the *in vivo* findings, further tissue immunostaining studies were conducted to include the non-lung tissues exhibiting uptake of 472. A weak signal was detected in formaldehyde-fixed spleen but not other tissues. When specimens were fixed more mildly with acetone, it was evident that mAb 472 stained blood microvessels in lung, kidney, adrenal gland and spleen, but not heart, liver, intestine, brain, muscle and testes. This tissue distribution supports the above *in vivo* findings. Again, mAb 833 stained microvascular endothelium only in the lung.

(*Id.* at 39-41.)

12. Based on the results in Example 8, the Specification states that "[t]hese organ-specific antibodies demonstrate that accessible, organ-

specific targets exist on the endothelial cell surface *in vivo*, and provide a means for localization or targeting of agents to specific organs or tissues, including targets in normal and diseased tissues" (*id.* at 41).

13. In Example 9, the Specification discloses perfusing mAb 833 conjugated to colloidal gold particles (TX3.833-Au) through the rat pulmonary artery. Analysis "revealed specific and rapid TX3.833-Au targeting to caveolae followed by transendothelial transport of the targeted cargo." (*Id.* at 45-46.)

14. The Specification, in Example 9, also discloses: "To test TX3.833 as a targeting vector, it was conjugated to various drugs and examined in vivo delivery of the immunoconjugate relative to the native drug. All TX3.833-drug conjugates showed greatly increased lung targeting up to 172-fold greater than drug alone." (*Id.* at 49.)

15. The Specification also states:

> The concept of vascular targeting has evolved in the last 20 years from the failure of many directed therapies to reach their intended target tissue cells. . . . Targeting endothelium because of its inherent IV accessibility has potential but so far requires key "proof of principle" in vivo. Although many attempts have been made to identify tissue-specific targets on vascular endothelium and to develop tissue-specific probes for vascular targeting . . . , directed delivery in vivo has not met theoretical expectations. . . . TX3.833 as a probe has the specificity and affinity as well as the tissue- and cell-selectivity to validate, for the first time, the vascular targeting strategy by achieving theoretical expectations with high-level tissue targeting in vivo. Perhaps more importantly, it targets dynamic caveolae to overcome the endothelial cell barrier for access to underlying tissue cells.

(*Id.* at 51-52.)

16. In addition, the Specification states:

> The cumulative in vivo and in situ data show that: i) caveolae can contain a tissue-specific endothelial protein, ii) an antibody can selectively and rapidly target and enter caveolae of microvascular endothelium in a specific tissue, and iii) targeting caveolae greatly increases the transendothelial transport and tissue accumulation over control antibodies (TTI $\geq$ 150). Little transport or tissue accumulation is observed with physically similar, isotype-matched control antibodies that differ from TX3.833 in their ability to recognize a specific caveolar antigen. Thus, it is the specific entry and binding within the caveolae, and not just binding to the endothelial cell surface or another microdomain, such as lipid rafts, nor fluid-phase uptake by the caveolae that mediate the rapid and selective transendothelial transport of TX3.833-Au. The graded, time-dependent movement of the caveolae-targeting immunoprobes across the cell barrier cannot be explained by a nonspecific transport pathway (i.e. intercellular junctions) and back-filling of the abluminal aspect of a static, branched caveolar system. . . . It is now clear from appropriate controls that caveolae can mediate selective transendothelial transport, although the exact mechanism for this transcytosis requires further elucidation.

(*Id.* at 52-53.)

17. Appellant relies on the following evidence:

ZhaoLan Tang et al., *Molecular Cloning of Caveolin-3, a Novel Member of the Caveolin Gene Family Expressed Predominantly in Muscle*, 271 THE JOURNAL OF BIOLOGICAL CHEMISTRY 2255-2261 (1996) (hereinafter "Tang");

Olivier Feron et al., *Dynamic Targeting of the Agonist-stimulated m2 Muscarinic Acetylcholine Receptor to Caveolae in Cardiac Myocytes*, 272 THE JOURNAL OF BIOLOGICAL CHEMISTRY 17744-17748 (1997) (hereinafter "Feron"); and

Philipp E. Scherer et al., *Cell-type and Tissue-specific Expression of Caveolin-2*, 272 THE JOURNAL OF BIOLOGICAL CHEMISTRY 29337-29346 (1997) (hereinafter "Scherer") (Reply Br. 2).

18. Tang discloses that "[c]aveolin-3 mRNA is expressed predominately in muscle tissue types (skeletal muscle, diaphragm, and heart)" (Tang, Abstract).

19. Feron discloses the "recent development of antibodies directed against different tissue-specific isoforms of caveolin" (Feron 17745).

20. Feron also discloses that "the dynamic targeting of agonist-stimulated muscarinic cholinergic receptors to caveolae in cardiac myocytes could facilitate the activation of eNOS [the endothelial isoform of nitric-oxide synthase], which we have shown to be quantitatively and specifically associated with caveolin-3, the muscle-specific isoform of caveolin" (*id.*).

21. Scherer examined the cell-type and tissue-specific expression of caveolin-2. Scherer discloses that "caveolin-2 protein is most abundantly expressed in endothelial cells, smooth muscle cell, skeletal myoblasts . . . , fibroblasts, and 3T3-L1 cells differentiated to adipocytes." (Scherer, Abstract.)

ENABLEMENT

Principles of Law

"It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art." *In re Sneed*, 710 F.2d 1544, 1548 (Fed. Cir. 1983). The doctrine of claim

differentiation creates a presumption that each claim in a patent has a different scope. *Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998).

"The first paragraph of 35 U.S.C. § 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention . . . without 'undue experimentation.'" *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991) (citing *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988)). Some experimentation, even a considerable amount, is not "undue" "if it is merely routine, or if the specification . . . provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands, supra*. In particular, "sufficient disclosure . . . to teach those of ordinary skill how to make and how to use the invention . . . means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." *In re Vaeck*, 947 F.2d at 496.

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *In re Wands, supra*. Factors to be considered include:

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id.

In unpredictable art areas, the Federal Circuit has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. *See, e.g., In re Goodman*, 11 F.3d 1046, 1050-52 (Fed. Cir. 1993); *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d. 1200, 1212-14 (Fed. Cir. 1991), cert. denied, 502 U.S. 856 (1991); *In re Vaeck*, 947 F.2d at 496. Enablement is lacking in those cases, the court has explained, because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation. *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

Analysis

Claims must be enabled throughout their claim scope. Thus, prior to analyzing the issue of enablement in the present case, the scope of the claims must be determined. Giving claim 3 its broadest reasonable interpretation in view of the Specification, and applying the principles of the doctrine of claim differentiation, we find that claim 3 is broader than claims 4, 12, and 14. Thus claim 3 encompasses embodiments disclosed in the specification and in the original claims wherein the agent of interest comprises a transport agent component which may be an antibody, a peptide, an inactivated virus, a receptor, a ligand, or a nucleic acid, as well as tissues including pulmonary, cardiac, cerebral, nephric, hepatic, endocrinous, and intestinal tissue.

The Examiner finds:

> [T]he specification teaches and exemplifies a rat lung-, microvessel-, and caveolae specific monoclonal antibody, Mab 833, which targets rat lung *in vivo* (p. 49), which targets a 90 kDa rat lung component of caveolae. The specification states that the concept of vascular targeting has evolved in the last 20 years from the failure of many directed therapies to reach their intended target cells (p. 51). Although many attempts have been made to identify tissue-specific targets on vascular endothelium and to develop tissue-specific probes for vascular targeting, directed delivery *in vivo* has still not met theoretical expectations (para bridging pages 51-52).

(Ans. 5.) However, the Examiner finds:

> [T]hese teachings are not considered enabling for the broadly claimed invention because the identification of Mab 833 as a rat lung specific binder to a rat lung specific component of caveolae was a hoped for but unexpected event. The discovery was unexpected because in 20 years of research by the combined efforts of those skilled in the art, this type of effective specificity had not been previously attained. Given the unexpected nature of the Mab 833 discovery, the identification of Mab 833 would not lead to other agents without undue experimentation.

(*Id.*) In addition, the Examiner finds that "the teaching of the single caveolae specific 90 kDa rat lung antigen does not predictably enable the broadly claimed invention since there is no teaching of any other tissue specific component that can be found in any species or tissues other than rat lung" (*id.*).

Appellant argues:

> The identification of Mab 833 exemplifies the methods that one of ordinary skill in the art can utilize to identify other tissue-specific antibodies. One of ordinary skill in the art, given the teachings of the specification, would understand that the

> important characteristic of an antibody, or any other agent for use in the methods, is that it binds to and localizes to a component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface. The specification details how to test antibodies or other agents for such specificity. While a certain amount of experimentation may be necessary to identify an antibody or agent having this desired characteristic, there is sufficient evidence in the Specification to guide one of ordinary skill in the art as to how to identify such an antibody or agent. . . . Thus, one of ordinary skill in the art, using no more than routine experimentation, would be able to apply the methods of the invention to other antibodies or agents of interest which bind to and localize to components of the caveolae, for tissue-specific targeting of agents.

(App. Br. 6.)

We conclude, upon review and weighing of the Wands factors in the present case, that the Examiner has the better argument. It is undisputed that the Specification discloses a technique that was used to identify an antibody, mAb 833, that binds to and localizes to a tissue-specific component of caveolae of the luminal surface of the vascular endothelium in the lung (*see* Findings of Fact (FF) 10-12). In addition, it is undisputed that the Specification discloses that, upon contact with the luminal surface of vascular, this antibody is delivered across the luminal surface of the vascular endothelium and from one side of an underlying cell to another side (*see* FF 7, 11, 13, & 14). However, the Specification does not disclose that these techniques can be reproducibly used to obtain additional antibodies or other agents, such as a peptide, an inactivated virus, a receptor, a ligand, or a nucleic acid, specific to other tissues that would be delivered across the luminal surface of the vascular endothelium and from one side of an

underlying cell to another side. The Specification does not provide specific examples of the claimed invention where the transporting agent is a peptide, an inactivated virus, a receptor, a nucleic acid, or a ligand other than an antibody. Nor does the Specification provide specific examples where the agent binds to a component of caveolae of vascular endothelium that is specific for cardiac, cerebral, nephric, hepatic, endocrinous, or intestinal tissue.

In an unpredictable art area such as that before us (FF 15), we do not find the broad generic claims to be enabled by a specification that demonstrates the enablement of only one or a few embodiments and does not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim. Enablement is lacking in this case because the undescribed embodiments cannot be made, based on the disclosure in the specification, without undue experimentation.

We recognize that the types of experiments disclosed in the Specification may be routine in the art (FF 5, 9, & 10). However, given the lack of predictability as to whether these techniques could successfully be used to obtain antibodies (much less other agents) specific to other tissues that would be delivered across the luminal surface of the vascular endothelium and from one side of an underlying cell to another side, we agree with the Examiner that the Specification does not enable the full scope of claim 3.

Appellant additionally argues that "it has been established previously that caveolae differ from tissue to tissue, and that certain proteins may be expressed primarily or solely in caveolae of certain types of tissues" (Reply

Br. 2). In support of this position, Appellant relies on Tang, Feron, and Scherer (*id.*). Based on this evidence, Appellant argues that "[o]ne of ordinary skill in the art would thus be aware that caveolae components *can* be tissue-specific" (*id.* (emphasis added)). Therefore, Appellant argues "that undue experimentation would not be required to make and utilize agents that bind and localize to a component of caveolae in a tissue-specific manner" (*id.*).

We are not persuaded. Appellant provides evidence that caveolin can be cell and tissue specific (FF 17-21). However, Appellant has not provided sufficient evidence that caveolin is specific among vascular endothelial cells, the cell type that is targeted in claim 3. The Specification does not provide specific examples where the agent binds to a component of caveolae of vascular endothelium that is tissue specific for cardiac, cerebral, nephric, hepatic, endocrinous, or intestinal tissue, within the scope of claim 3.

Thus, we do not agree that Appellant has provided sufficient evidence to rebut the Examiner's prima facie case that the full scope of claim 3 is not enabled.

Conclusion

Appellant has not demonstrated that the Examiner erred in concluding that claim 3 is not enabled. We therefore affirm the enablement rejection of claim 3. Claims 4, 5, 7-9, and 12-14 fall with claim 3.

WRITTEN DESCRIPTION

Principles of Law

The first paragraph of 35 U.S.C. § 112 "requires a 'written description of the invention' which is separate and distinct from the enablement requirement." *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991). An adequate written description of a chemical invention "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 927 (Fed. Cir. 2004); *Regents of the Univ. of Cal. v. Eli Lilly & Co., Inc.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997); *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). "A description of what a material does, rather than of what it is, usually does not suffice." *Rochester*, 358 F.3d at 923; *Eli Lilly*, 119 F.3d at 1568. Instead, the "disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described." *Id.* However, not all functional descriptions "necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1332 (Fed. Cir. 2003).

> The "written description" requirement . . . serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. . . . The descriptive text needed to meet these requirements varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence.

Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir. 2005). "The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge." *Id.*

Analysis

The Examiner finds:

> The written description . . . only sets forth a method of delivering an agent of interest comprising Mab 833 across a luminal surface of vascular endothelium from one side of an underlying cell to another side by binding to a component of caveolae, a 90 kDa antigen, on the luminal surface of the vascular endothelium and . . . is not commensurate in scope with the claims drawn to a method of delivering any agent of interest across a luminal surface of vascular endothelium from one side of an underlying cell to another side in a tissue specific manner by binding to any component of caveolae on the luminal surface of the vascular endothelium in a tissue.

(Ans. 6.) In particular, the Examiner finds:

> The instant invention fails to meet the Written Description standards because the specification describes the broadly claimed agent of interest and the broadly claimed target of the agent of interest only by function - that is that the target is a tissue-specific component of caveolae and that the agent of interest binds to said target. . . . Since the disclosure fails to describe the common attributes or characteristics that identify the members of the genus and because the genus is highly variant, the disclosure of a single specific agent of interest and the ability to screen, as taught in the specification is insufficient to describe the genus.

(*Id.* at 6-7.)

Appellant argues that the characteristic of "binding to a component of caveolae of the luminal surface of the vascular endothelium, in a tissue-

specific manner[,] . . . is sufficient to distinguish the claimed material from other materials" (App. Br. 7-8).

We conclude that the Examiner has the better argument. Claim 3 recites "an agent of interest that binds to and localizes to a [tissue-specific] component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface." We agree with the Examiner that, based on Federal Circuit precedent, the functional property of binding to and localizing to a tissue-specific component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface is insufficient to provide written descriptive support for all agents within the scope of the claims having this functional characteristic. In particular, Appellant has not shown that this functional characteristic "is sufficiently correlated to a particular, known structure" in order to describe agents having this function. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d at 1332.

Because Appellant has not shown that the claimed functional characteristic of binding to and localizing to a tissue-specific component of caveolae of the luminal surface of the vascular endothelium is sufficiently correlated to a structure of the agents of interest, an adequate written description of the agents of interest claimed requires a precise definition, such as by structure, formula, chemical name, or physical properties of the agents. The Specification does not specifically describe agents of interest that comprise a transport agent component that is a peptide, an inactivated virus, a receptor, a nucleic acid, or a ligand other than an antibody. Nor does the Specification specifically describe a method as claimed wherein the

agent binds to a component of caveolae of vascular endothelium that is specific for cardiac, cerebral, nephric, hepatic, endocrinous, or intestinal tissue.

Appellants have not shown that the functional property of binding to and localizing to a tissue-specific component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface is sufficient to provide written descriptive support for all agents within the claim scope having this functional characteristic. We find that, in view of the unpredictability of the state of the art (FF 15) and in view of the context of the present invention in the state of the art, more description is required to support the pending claim scope.

Conclusion

Appellant has not demonstrated that the Examiner erred in concluding that claim 3 is not supported by an adequate written description. We therefore affirm the written description rejection of claim 3. Claims 4, 5, 7-9, and 12-14 fall with claim 3.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

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